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PATENT  
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS: Cauwenberghs *et al.*  
SERIAL NO.: 10/019,740 GROUP NO.: 1641  
FILING DATE: December 28, 2001 EXAMINER: Jung, Unsu  
TITLE: *Detection of von-Willebrand Factor (vWF) Activity*

Mail Stop RCE  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION OF DR. HANS DECKMYN UNDER 37 C.F.R. § 1.132**

Dear Sir:

I, Dr. Hans Deckmyn, hereby declare and state as follows:

1. I am a recognized expert in the field of von Willebrand's disease and have been working in this field for many years. My *curriculum vitae*, which includes my educational and employment history and a list of my publications and patents, is attached hereto as Exhibit A. My present position is Professor of Chemistry at KU Leuven Campus Kortrijk. I am also a board member of the Belgian Society on Thrombosis and Haemostasis and an executive officer of the European Thrombosis Research Organization.
2. I am a co-inventor of the subject matter claimed in the patent application U.S. Serial No. 10/019,740 ("the present application"). I understand that the present application has an effective filing date of July 5, 1999.
3. I have been asked to evaluate the following:

Whether the collagen-binding assay (CBA) and the ristocetin cofactor assay were art-recognized equivalents at the time of the invention in methods for measuring von Willebrand factor (vWF) activity and whether employing the CBA or the ristocetin

cofactor assay in a diagnostic method would materially affect the diagnosis of von Willebrand's disease?

My analysis in light of the state of the art at the time the present application was filed (1999) follows.

4. von Willebrand's disease is the most-common inherited bleeding disorder caused by defects or deficiencies in vWF. vWF is an adhesive plasma protein essential to hemostasis. vWF possesses multiple functions and activities. For example, during hemostasis and coagulation, vWF permits adhesion of platelets to sites of vascular damage. vWF also binds to tissue matrix proteins including collagen. In plasma, vWF exists in a multimeric dimer configuration, ranging in size from small multimers to large multimers. The larger the vWF molecule, the greater its adhesive capacity.
5. von Willebrand's disease is a heterogeneous disorder. Sometimes, it is caused by the absence of the larger multimers also known as high molecular weight (HMW) vWF multimers. Sometimes, it is caused by the reduction or absence of all forms of vWF multimers. On other occasions, it is caused by mutations on the vWF protein that affect its specific functions. Depending on the nature of the defects or deficiencies, von Willebrand's disease can be classified into three major categories, namely, types 1, 2 and 3. Type 2 von Willebrand's disease can be further divided into subtypes 2A, 2B, 2M and 2N. Subtype 2A is associated with decreased vWF-dependent platelet function due to absence of HMW vWF multimers. Subtype 2B is associated with increased affinity of vWF for platelet glycoprotein 1b (GP1b) and typically is also associated with loss of HMW vWF multimers. Subtype 2M is associated with decreased vWF-dependent platelet function not due to loss of HMW vWF multimers. Subtype 2N is associated with decreased affinity of vWF for factor VIII but has normal vWF-dependent platelet function.
6. The precise diagnosis of types and subtypes of a patient's von Willebrand's disease is crucial in assessing the hemorrhagic risk and determining optimal therapeutic treatment for the patient. The precise diagnosis of von Willebrand's disease, in turn, requires comprehensive laboratory and/or clinical testing. Because of the heterogeneous nature of von Willebrand's disease, no single assay is robust enough to permit detection of all von

Willebrand's disease types and subtypes in a patient. Due to limitations of each assay, a test panel is therefore required to pinpoint specific defects entailed on vWF.

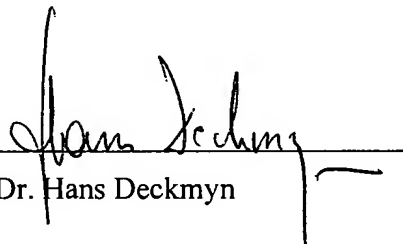
7. At the time the present application was filed (1999), a number of diagnostic assays were known which detect different properties of vWF, among which were the CBA and the ristocetin cofactor assay. The following paragraphs describe the state of art in 1999 with respect to the CBA and the ristocetin cofactor assay.
  - a. The CBA method measures the ability of vWF to bind to collagen, *i.e.*, the collagen-binding activity. The ristocetin cofactor assay, on the other hand, measures a specific vWF activity, *i.e.*, the ability of vWF to bind to the GPIb complex present on the surface of platelets in the presence of ristocetin or botrocetin (*i.e.*, the platelet GPIb-binding activity), which reflects the platelet adhesion and/or aggregation function of vWF in plasma. Therefore, the CBA and the ristocetin cofactor assay measures clearly distinct vWF activities associated with distinct biochemical functions.
  - b. At the molecular level, it was known in 1999 that the collagen-binding activity of vWF primarily involves the functional domain A3 of mature vWF. The platelet GPIb-binding activity of vWF primarily involves the functional domain A1. Mutations in functional domain A1 were known to be associated with a number of variants in subtypes 2A, 2B and 2M of von Willebrand's disease, while no mutations in functional domain A3 were known to be associated with any subtypes of von Willebrand's disease in 1999.
  - c. Procedurally, the CBA method uses ELISA test to measure the collagen-binding activity of vWF using immobilized collagen. The assay was developed based on collagen's selective ability to primarily recognize HMW vWF multimers. The CBA method, however, detects only some 30% of total vWF present in plasma. As a result, the CBA method provides very good information on the HMW multimers of vWF present, but does not provide a good estimate of total level of vWF. The ristocetin cofactor assay, on the other hand, uses ristocetin-induced platelet aggregation or agglutination procedure to measure the platelet GPIb-binding activity of vWF. The ristocetin cofactor assay provides an estimate of the total level of vWF present and additional information on the quality of vWF present related to the size of multimers and specific functional defects. Thus, whereas both the CBA

method and the ristocetin cofactor assay are capable of detecting patients with subtypes 2A and 2B von Willebrand's disease due to the absence of HMW vWF multimers in the patients' plasma, only the ristocetin cofactor assay is sensitive in detecting patients with subtype 2M due to functionally defective vWF unrelated to a loss of HMW vWF forms.

8. Accordingly, the CBA and the ristocetin cofactor assay were not art-recognized equivalents at the time of the invention for measuring vWF activity. Employing the CBA or the ristocetin cofactor assay materially affects the diagnosis of von Willebrand's disease.

9. I further declare that all statements made in this Declaration are of my own knowledge, are true, and that all statements made on information and belief are believed to be true. Moreover, these statements were made with the knowledge that willful false statements and the like made by me are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: 15 February 2007

By:   
Dr. Hans Deckmyn

02/21/2007

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Exhibit A

EV 928084169<sup>1</sup> US

## Curriculum Vitae Hans DECKMYN

Born: February 5, 1953 - Roeselare, Belgium  
Married to Liesbeth Lybeer  
Children: Ilse (1980), Sam (1982), Thomas (1984)  
Home address: Lemingstraat 1, B-3210 Linden (Belgium)  
tel: 32 16 256694

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Interdisciplinary Research Center  
KU Leuven, Campus Kortrijk  
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## Education

High-School: Latin-Science, Klein Seminarie, Roeselare  
  
University: 1974: Bachelor in Chemistry, KU Leuven, Campus Kortrijk  
1976: Biochemist, KU Leuven  
1980: Ph.D. Biochemistry, KU Leuven

Military service: 1980 (february-november)

## Professional positions

1977: Part-time assistant, KU Leuven  
  
1977-1980: Doctoral student Laboratory for Biochemistry (Prof. G.Préaux)  
  
1981-1985: Postdoc Center for Thrombosis and Vascular Research, (Prof. M. Verstraete, Prof. J. Vermynen)  
  
1985-1987: Postdoc Division of Hematology-Oncology, Washington University School of Medicine, St.Louis Mo, USA (Prof. P.W. Majerus),  
  
1988-1992: Senior Researcher (eerstaanwezend assistent) Center for Molecular and Vascular Biology KU Leuven (Prof. D. Collen, Prof. J. Vermynen)  
  
1992-1996: Associate Professor in Chemistry (hoofddocent) KU Leuven Campus Kortrijk  
  
1994-present: Head of the Laboratory for Thrombosis Research, IRC, KU Leuven Campus Kortrijk  
  
1996-1999: Professor in Chemistry (hoogleraar) KU Leuven Campus Kortrijk  
  
1999-present: Full Professor in Chemistry (gewoon hoogleraar) KU Leuven Campus Kortrijk

## other

2000-2006: Chairman Interdisciplinary Research Center (IRC), KU Leuven Campus Kortrijk  
2004-present Spokesman "Interfaculty Center for Biomacromolecular Structure Research" (BioMacS) KU Leuven <http://biomacs.kuleuven.be/index.htm>  
2002-present Board member 'Belgian Society on Trombosis and Haemostasis' (BSTH)  
2007-present Executive Officer 'European Thrombosis Research Organisation' (ETRO)  
2005-present Board member 'European Cardiovascular Genetics Institute' (ECGI)

## Awards

1978-1979:	Post-graduate fellowship I.W.O.N.L. (Institute for the Advancement of Scientific Research in Industry and Agriculture, Belgium)
1985:	Prize Boehringer-Ingelheim for Research on Thrombosis and Coagulation
1985-1987:	NATO Research Fellowship
1985-1986:	Fulbright Research Award
1989:	Young Investigator Award XIIth Congress on Thrombosis and Hemostasis
1991:	European Thrombosis Research Organisation (ETRO) Travel grant
1991:	Prize "Dr. en Mevr. Schamelhout-Koettlitz "-Foundation for Scientific Research (Royal Academy of Medicine of Belgium)
1992	Fellowship "Belgian Action against Cancer"
1993	Triannual Prize Baron Simonart Foundation for Clinical Pharmacological Research
1995	Awardee Research grant O.Dupont Foundation (Royal Academy of Medicine of Belgium)
1997	Visiting professor "Pro Renovanda" University of Debrecen, Hongarije, Medical School
2004:	Triannual price <i>Sidmar</i> for 'Medical Scientific Research' Royal Academy for Medicine of Belgium

## Memberships, meetings, journals

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### 1. *International Society on Thrombosis and Haemostasis (ISTH)*

1992-present::	Member
1992-8:	Associate Editor Journal of the Society: "Thrombosis and Haemostasis"
1997-8:	Co-chairman of Scientific and Standardisation Committee, Subcommittee on "Platelet Physiology"
1999:	Member Advisory Board " <i>Thrombosis and Haemostasis</i> ".
1998-present:	Member of the International Advisory Committee for the XVII, XVIII, XIXth Congress of the ISTH, Washington 1999, Parijs 2001, Birmingham 2003, Geneve 2007
2007:	Invited speaker Geneve

### 2. *Biochemical Society*

1994-present:	member
1994-1998:	Editorial Advisor of "The Biochemical Journal"
1998-2003:	Editor of "The Biochemical Journal"

### 3. *European Thrombosis Research Organisation (ETRO)*

1995-present:	Laboratory for Thrombosis Research, IRC-KULAK elected member
1997:	Invited speaker ETRO Advanced Teaching Course, Heviz, Hungary
2003:	Invited speaker ETRO Advanced Teaching Course, Blankenberge, Belgium
2007-10:	Executive Officer

4. *Belgian Society on Thrombosis and Haemostasis (BSTH)*

1993-present: member

5. *Vlaamse Leergangen*

1997-present: member

6. *Koninklijke Vlaams Chemische Vereniging*

1998- present: member

Member Scientific Committee European Platelet and Granulocyte Immunobiology Symposium  
(Bamberg, Germany 1992, Cambridge, UK 1994, Hammeenlinna, Finland 1996,  
S'Agaro, Spain, 1998, Amsterdam, 2000)

2007-9 Section Editor: Thrombosis and Haemostasis

Regular reviewer for:

Circulation; Blood; Journal of the American College of Cardiology; Thrombosis and Haemostasis; Thrombosis Research; Biochemical Journal; Arteriosclerosis, Thrombosis and Vascular Biology;

Occasional reviewer for:

European Heart Journal; Fibrinolysis; Journal of Cardiovascular Pharmacology; Hypertension in Pregnancy; Diabetes Research and Clinical Practice; Life Sciences; European Journal of Clinical Investigation; British Journal of Pharmacology; Biochimica et Biophysica Acta; Blood Coagulation & Fibrinolysis; European Journal of Biochemistry

### Patent applications

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1. "Detection of von-Willebrand factor (vWF) activity"

EP patent Application, Roche Diagnostics 7/1999

Inventors: N. Cauwenberghs, K. Vanhoorelbeke, H. Deckmyn

2. "An anti-GPIIb inhibitory monoclonal antibody as an antithrombotic compound"

EP Patent Application, Leuven R&D, 1/2000

Inventors: N. Cauwenberghs, H. Deckmyn

3. "Inhibition of the vWF-collagen interaction by anti-human vWF monoclonal antibody (82D6A3) results in abolition of in vivo arterial thrombus formation in baboons.

EP provisional patent application, Thromb-X

Inventors : K. Vanhoorelbeke, N. Cauwenberghs, H. Deckmyn

4. "High-throughput platelet function test"

EP provional patent application: ECGF

Inventors: H Deckmyn, I Salles, A Fontayne

### Onderwijs/Teaching

1992-present: Introductory course 'General Chemistry': 1<sup>st</sup> yr students Medicine, Biomedical Sciences, Biochemistry, Biology, Chemistry, Physics, Mathematics (~180/yr)

1992-2003: Chemistry II (Systematics) 1<sup>st</sup> yr students Biochemistry, Chemistry, Biology

1996-2000: Mechanisms of signal transduction, PhD-training Sciences-Bioengineers-Pharmacy-Biomedical Sciences

1999-present: Cell Biology (part signal Transdcution) : 1<sup>st</sup> yr students Medicine, Biomedical Sciences (~100/yr)

2005-present: Biochemistry: 1<sup>st</sup> yr students Biochemistry, Chemistry, Biology,

## Publicatielijst/Publication list

### I/ Internationale tijdschriften/ International Journals

1. Defreyne G, Deckmyn H, Vermynen J.  
A thromboxane synthetase inhibitor reorients endoperoxide metabolism in whole blood towards prostacyclin and prostaglandin E2.  
**Thromb. Res.** 26, 389-400, 1982
2. Badenhorst PN, Deckmyn H, Vermynen J.  
The effect of sulphinpyrazone on whole blood thromboxane and prostacyclin generation in man.  
**Thromb. Res.** 28, 59-66, 1982.
3. Boogaerts MA, Vermynen J, Deckmyn H, Roelant C, Verwilghen RL, Jacobs HS, Moldow CF.  
Enkephalins modify granulocyte-endothelial interactions by stimulating prostacyclin production.  
**Thromb. Haemost.** 50, 572-575, 1983.
4. Deckmyn H, Proesmans W, Vermynen J.  
Prostacyclin production by whole blood from children: impairment in the hemolytic uremic syndrome and excessive formation in chronic renal failure.  
**Thromb. Res.** 30, 13-18, 1983.
5. Spitz B, Deckmyn H, Van Assche FA, Vermynen J.  
Prostacyclin production in whole blood throughout normal pregnancy.  
**Clin.Exp.Hypert.-Hypert. in Pregnancy** B2, 191-202, 1983.
6. Vermynen J, Badenhorst PN, Deckmyn H, Arnout J.  
Normal mechanisms of platelet function.  
**Clin. Haematol.** 12, 107-151, 1983.
7. Vermynen J, Deckmyn H.  
Reorientation of prostaglandin endoperoxide metabolism by a thromboxane synthetase inhibitor: in vitro and clinical observations.  
**Br.J.Clin.Pharmacol.** 15, 17S-22S, 1983.
8. Deckmyn H, Font L, Van Hemelen C, Carreras LO, Defreyne G, Vermynen J.  
Low prostacyclin synthetase activity of fetal rat aorta.  
**Life Sci.** 33, 1491-1497, 1983.
9. Deckmyn H, Van Houtte E, Verstraete M, Vermynen J.  
Manipulation of the local thromboxane and prostacyclin balance in vivo by the antithrombotic compounds dazoxiben, acetylsalicylic acid and nafazatrom.  
**Biochem. Pharmacol.** 32, 2757-2762, 1983.
10. Gresele P, Zoja C, Deckmyn H, Arnout J, Vermynen J, Verstraete M.  
Dipyridamole inhibits platelet aggregation in whole blood.  
**Thromb. Haemost.** 50, 852-856, 1983.
11. Van Assche FA, Spitz B, Vermynen J, Deckmyn H.  
Preliminary observations on treatment of pregnancy induced hypertension with a thromboxane synthetase inhibitor.  
**Am. J. Obstet. Gynecol.** 148, 216-218, 1984.



12. Boogaerts MA, Van de Broeck J, Deckmyn H, Roelant C, Vermylen J, Verwilghen RL. Protective effect of vitamin E on immune triggered granulocyte mediated endothelial injury.  
*Thromb. Haemost.* 51, 89-92, 1984.
13. Deckmyn H, Gresele P, Arnout J, Vermylen J.  
BM 13.177 specifically blocks the platelet thromboxane receptor.  
*Arch. Intern. Pharmacodynam. Ther.* 268, 165-166, 1984.
14. Essien EM, Arnout J, Deckmyn H, Vermylen J, Verstraete M.  
Blood changes and enhanced thromboxane and 6-keto prostaglandin F<sub>1</sub> $\alpha$  production in experimental acute plasmodium bergi infection in hamsters.  
*Thromb. Haemost.* 51, 362-365, 1984.
15. Gresele P, Deckmyn H, Arnout J, Vermylen J.  
Platelet inhibitory activity of prostacyclin in the presence of erythrocytes as studied with the impedance aggregometer.  
*Br. J. Haemat.* 57, 171-173, 1984.
16. Gresele P, Deckmyn H, Huybrechts E, Vermylen J.  
Serum albumin enhances the impairment of platelet aggregation with thromboxane synthase inhibition by increasing the formation of prostaglandin D<sub>2</sub>.  
*Biochem. Pharmacol.* 33, 2083-2088, 1984.
17. Gresele P, Deckmyn H, Arnout J, Lemmens J, Janssens W, Vermylen J.  
BM 13.177, a selective blocker of platelet and vessel wall thromboxane receptors, is active in man.  
*Lancet* i, 991-994, 1984.
18. Deckmyn H, Gresele P, Arnout J, Todisco A, Vermylen J.  
Prolonging prostacyclin production by nafazatrom and dipyridamole.  
*Lancet* ii, 410-411, 1984.
19. Spitz B, Deckmyn H, Van Assche FA, Vermylen J.  
Prostacyclin in pregnancy.  
*Eur. J. Obstet. Reprod. Biol.* 18, 303-308, 1984.
20. Arnout J, Vanrusselt M, Deckmyn H, Vermylen J, Fiocchi R, Lijnen P, Amery A.  
Platelet hypersensitivity to serotonin after prolonged ketanserin intake?  
*J. Cardiovasc. Pharmacol.* 7 (suppl.7), S20-S22, 1985.
21. Ceuppens JL, Vertessen S, Deckmyn H, Vermylen J.  
Effects of thromboxane A<sub>2</sub> on lymphocyte proliferation.  
*Cell. Immunol.* 90, 458-463, 1985.
22. De Maeyer P, Deckmyn H, Arnout J, Vermylen J.  
Intravenous ionic contrast media cause local prostacyclin release in man  
*Investigative Radiol.* 20, 458-463, 1985.
23. Deckmyn H, Zoja C, Arnout J, Todisco A, D'Hondt J, Vanden Bulcke F, Hendrickx N, Gresele P, Vermylen J.  
Partial isolation and function of the prostacyclin regulating plasma factor.  
*Clin. Sc.* 69, 383-393, 1985.
24. Gresele P, Arnout J, Deckmyn H, Vermylen J.  
Combining antiplatelet agents: potentiation between aspirin and dipyridamole.  
*Lancet* i, 937-938, 1985.

25. Gresele P, Bounameaux H, Arnout J, Perez-Requejo JL, Deckmyn H, Vermylen J. Thromboxane A<sub>2</sub> and prostacyclin do not modulate the systemic hemodynamic response to cold in humans. *J. Lab. Clin. Med.* 106, 534-541, 1985.
26. Janssens WJ, Deckmyn H, Gresele P, Vermylen J. BM 13.177 selectively inhibits endoperoxide analog induced vascular contractions. *Arch. Intn'l Pharmacodyn. Ther.* 276, 28-34, 1985.
27. Spitz B, Deckmyn H, Van Bree R, Pijnenborg R, Vermylen J, Van Assche FA. Influence of a vitamin E deficient diet on prostacyclin production by mesometrial triangles and aortic rings from non-diabetic and diabetic rats. *Am. J. Obstet. Gynecol.* 151, 116-120, 1985.
28. Van Renterghem Y, Roels L, Lerut T, Gruwez J, Michielsen P, Gresele P, Deckmyn H, Colucci M, Arnout J, Vermylen J. Thrombo-embolic complications and haemostatic changes in cyclosporin-treated cadaveric kidney transplants. *Lancet* i, 999-1002, 1985.
29. Gresele P, Deckmyn H, Arnout J, Zoja C, Vermylen J. Lack of synergism between dazoxiben and dipyridamole following administration to man. *Thromb. Res.* 37, 231-236, 1985.
30. Vermylen J, Deckmyn H, Arnout J, Gresele P. A. Schmidt Memorial Lecture: Peroxides in haemostasis and thrombosis. *Haemostasis* 15, 8-9, 1985.
31. Vervliet G, Deckmyn H, Carton H, Billiau A. Influence of prostaglandin E<sub>2</sub> and indomethacin on interferon-gamma production by cultured peripheral blood leukocytes of multiple sclerosis patients and healthy donors. *J. Clin. Immunol.* 5, 102-108, 1985.
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33. Vermylen J, Arnout J, Deckmyn H, Xhonneux B, De Clerck F. Continuous inhibition of the platelet S<sub>2</sub>-serotonergic receptors during the long term administration of ketanserin. *Thromb. Res.* 42, 721-723, 1986.
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35. Gresele P, Arnout J, Coene MC, Deckmyn H, Vermylen J. Leukotriene B<sub>4</sub> production by stimulated whole blood: comparative studies with isolated polymorphonuclear cells. *Biochem. Biophys. Res. Commun.* 137, 334-342, 1986.
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37. Deckmyn H, Tu SM, Majerus PW. Guanine nucleotides stimulate soluble phospholipase C in the absence of membranes. *J. Biol. Chem.* 261, 16553-16558, 1986.

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39. Kienast J, Arnout J, Deckmyn H, Pfliegler G, Hoet B, Vermynen J. On the role of guanine nucleotide binding regulatory proteins (G-proteins) in signal transduction in human platelets: studies with sodium fluoride (NaF). **Agents Actions**, Suppl. 20, 175-180, 1986.
40. Kienast J, Arnout J, Pfliegler G, Deckmyn H, Hoet B, Vermynen J. Sodium fluoride mimics effects of both agonists and antagonists on intact human platelets by simultaneous modulation of phospholipase C and adenylate cyclase activity. **Blood** 69, 859-866, 1987.
41. Gresele P, Arnout J, Deckmyn H, Huybrechts E, Pieters G, Vermynen J. Role of proaggregatory and antiaggregatory prostaglandins in hemostasis. Studies with combined thromboxane synthase inhibition and thromboxane receptor antagonism. **J. Clin. Invest.** 80, 1435-1445, 1987.
42. Arnout J, Kienast J, Deckmyn H, Vermynen J. Prostacyclin stimulatory activity of reducing cofactors in human plasma filtrate. A potential role for uric acid. **Agents and Actions** 22, 360-361, 1987.
43. Gresele P, Arnout J, Deckmyn H, Vermynen J. L-652,343, a novel dual cyclo/lipoxygenase inhibitor, inhibits LTB<sub>4</sub>-production by stimulated human polymorphonuclear cells but not by stimulated whole blood. **Biochem. Pharmacol.** 36, 3529-3532, 1987.
44. Arnout J, Van Russelt M, Deckmyn H, Vermynen J. Continuous inhibition of serotonin-induced platelet aggregation during chronic ketanserin administration to man can be detected after plasma pH control. **Haemostasis** 17, 344-348, 1987.
45. Gresele P, Blockmans D, Deckmyn H, Vermynen J. Adenylate cyclase activation determines the effect of thromboxane synthase inhibitors on platelet aggregation in vitro. Comparison of platelets from responders and non-responders. **J Pharmacol. Exp. Ther.** 246, 301-307, 1988.
46. Falcon C, Pfliegler G, Deckmyn H, Vermynen J. The platelet insulin receptor: detection, partial characterization, and search for a function. **Biochem. Biophys. Res. Comm.** 157, 1190-1196, 1988.
47. Van Geet C, Deckmyn H, Kienast J, Wittevrongel C, Vermynen J. Dual effect of fluoride on endothelial prostacyclin production: a phospholipase C mediated phenomenon. **Prog. Clin. Biol. Res.** 301, 377-381, 1989.
48. Gresele P, Deckmyn H, Arnout J, Nenci GG, Vermynen J. Characterization of N,N'-bis(3-picolyl)-4-methoxy-isophtalamide (picotamide) as a dual thromboxane synthase inhibitor/thromboxane A<sub>2</sub> receptor antagonist in human platelets. **Thromb. Haemost.** 61, 479-484, 1989.
49. Hoet B, Falcon C, De Reys S, Arnout J, Deckmyn H, Vermynen J. R68070, a combined thromboxane/endoperoxide receptor antagonist and thromboxane synthase inhibitor, inhibits human platelet activation in vitro and in vivo: a comparison with aspirin. **Blood** 75, 646-653, 1990.

50. Van Geet C, Deckmyn H, Kienast J, Wittevrongel C, Vermynen J.  
Guanine nucleotide-dependent inhibition of phospholipase C in human endothelial cells.  
*J. Biol. Chem.* 265, 7920-7926, 1990.
51. Deckmyn H, Chew SL, Vermynen J.  
Lack of platelet response to collagen associated with an autoantibody against glycoprotein Ia: a novel cause of acquired qualitative platelet dysfunction.  
*Thromb. Haemost.* 64, 74-79, 1990.
52. Hoet B, Arnout J, Van Geet C, Deckmyn H, Verhaeghe R, Vermynen J.  
Ridogrel, a combined thromboxane synthase inhibitor and receptor blocker, decreases elevated plasma beta-thromboglobulin levels in patients with documented peripheral arterial disease.  
*Thromb. Haemost.* 64, 87-90, 1990.
53. Hoet B, Deckmyn H, Arnout J, Vermynen J.  
Pharmacological manipulation of the thromboxane pathway in blood platelets.  
*Blood Coag Fibrinol.* 1, 225-234, 1990.
54. Kienast J, Arnout J, Deckmyn H, Van der Schueren B, Vermynen J.  
Non-receptor mediated refractoriness in prostacyclin production by human endothelial cells in a continuous flow system is delayed by a low molecular weight plasma fraction devoid of reducing cofactors for peroxide-catalyzed reactions.  
*Blood Coag Fibrinol.* 1, 609-618, 1990.
55. Stockmans F, Deckmyn H, Gruwez J, Vermynen J, Acland R.  
Continuous quantitative monitoring of mural, platelet-dependent, thrombus kinetics in the crushed rat femoral vein.  
*Thromb. Haemost.* 65, 425-431, 1991.
56. Tornai I, Declerck PJ, Smets L, Arnout J, Deckmyn H, Caekebeke-Peerlinck KMJ, Vermynen J.  
Measurement of von Willebrand factor antigen in plasma and platelets with an enzyme-linked immunosorbent assay based on two murine monoclonal antibodies.  
*Haemostasis* 21, 125-134, 1991.
57. Gresele P, Deckmyn H, Nenci GG, Vermynen J.  
Thromboxane synthase inhibitors, thromboxane receptor antagonists and dual blockers in thrombotic disorders.  
*TiPS (Trends Pharmacol. Sc.)* 12, 158-163, 1991.
58. Stockmans F, Deckmyn H, Vermynen J.  
Thrombosis in injured small vessels.  
*Plast. Reconstr. Surg.* 88, 174-175, 1991.
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